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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,076	09/07/2006	Bengt-Ake Bengtsson	05558.0036.PCUS00	2186

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EXAMINER	
BORGHEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

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04/08/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/595,076	BENGTSSON, BENGT-AKE	
	Examiner	Art Unit	
	Christina Borgeest	1649	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 March 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☒ Applicant's reply has overcome the following rejection(s): 5, 6, 8-13.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *5,6,8-13 and 39*.
   Claim(s) rejected: *1,14,15,18,25 and 33*.
   Claim(s) withdrawn from consideration: *28-30,36 and 37*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Bridget E Bunner/
Primary Examiner, Art Unit 1647

Continuation of 11. does NOT place the application in condition for allowance because: Applicants reply has overcome one of the issues raised in the Final Office action. Briefly, the amendment of the independent claim 1 to recite Multiple System Atrophy or MSA instead of Parkinsonism Plus Syndrome remedies the issues raised with respect to the breadth of treatment of Parkinsonism Plus Syndrome.

The remaining issue, which is maintained, is that Applicants are not enabled for treatment of MSA comprising administration of hGHRH. Briefly, claims 1, 14, 15, 18, 25 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the amelioration of the symptoms of Multiple Symptom Atrophy or MSA comprising administering to a person suffering from MSA a substance selected from the group consisting of (a) human growth hormone (hGH), (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH receptor, (c) a salt of (a) or (b), wherein administration of said substance ameliorates the symptoms of Multiple Symptom Atrophy or MSA, does not reasonably provide enablement for the claims as broadly recited. Specifically, as noted above, Applicants are not enabled for treatment of MSA comprising administration of hGHRH. Applicants argue that:

I. The scope of enablement must only bear a "reasonable correlation to the scope of the claims, citing In re Fisher, 427 F.2d 833, 839, 166, USPQ 18, 24 (CCPA 1970).

II. The Examiner has not provided evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility and has not established a prima facie case of lack of utility/operability under 35 U.S.C. 112, first paragraph, pointing out that one skilled in the art would recognize that hGHRH stimulates hGH, thus the biological activity of hGH can be directly obtained by adminstering GHRH or a functional derivative, citing paragraph 122 of the publication of the instant specification.

Regarding Argument I, it should be noted that the full quote from In re Fisher reads:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

This quote underscores the unpredictability of factors involving physiological activity, in general, and the unpredicitability of hGHRH in particular is explained further below.

Regarding Argument II, the Examiner has explained in the previous Office actions that the art is silent with respect to treatment of MSA with hGHRH, and the specification contains only a single paragraph, without working examples or guidance, as to how it would be predictable that hGHRH could treat MSA. Second, the specification and the art only teach a slight improvement of MSA symptoms resulting from hGH treatment, thus it would not be predictable that administration of hGHRH, a different molecule, would result in improvement. hGHRH is not equivalent to administration of GH because they are completely different molecules. While hGHRH stimulates GH release, it has its own biological effects which may not be compatible with treatment of MSA since hGHRH stimulates gastrin release and epithelial cell proliferation in the digestive tract, as well as insulin, glucagon, and somatostatin secretion from the pancreas. hGHRH can also inhibit TRH secretion and affect TSH and thyroid hormone. It is not predictable given the state of the art as outlined by Holmberg (previously cited by Examiner) that a molecule having these effects would ameliorate symptoms of MSA. Fourth, according to evidence submitted by Applicants on their IDS filed 7 November 2006, hGHRH administration is far less effective in older adults than hGH. See Ghigo et al. p. 162, left column, which notes the poor reproducibility of hGHRH, its dependence on gender and "marked age-related variations...the effect of which is maximal at birth and then progressivly decreases to a very low level of activity with aging." Furthermore, Camanni et al. (also submitted by Applicants on IDS filed 7 November 2006) teaches the inabilty of GHRH response in various types of conditions, pointing to the fact that hGHRH and hGH are not known equivalents. In summary, it is not predictable that blood plasma levels of GH would be achieved to give the therapeutic effect necessary in treating MSA, the treatment of which, as outlined in the previous Office actions, is itself unpredictable.

Since claims 5, 6, 8-13 and 39 are limited to hGH and its variants, these claims would be allowable if rewritten in independent form including all of the limitations of the base claim (minus the recitation hGHRH and its variants) and any intervening claims.